

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Gerald Koelsch, Jordan J. N. Tang, Lin Hong, and Arun K. Ghosh

Serial No.: Divisional of 09/603,713  
Express Mail Label  
No. EL 709 418 840 US  
Date of Deposit: April 30, 2001

Filed: April 30, 2001

For: INHIBITORS OF MEMAPSIN 2 AND USE THEREOF

BOX PATENT APPLICATION  
Assistant Commissioner for Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Sir:

Prior to examination, please amend the application as follows.

**In the Specification**

On page 1, line 3, after "This application", please insert --is a divisional of  
U.S.S.N. 09/603,713 filed June 27, 2000, by Jordan J. N. Tang and Arun K. Ghosh which--.

On page 7, line 20, please delete "Figure 3", and insert --Figures 3A and 3B-- in place  
thereof.

On page 7, line 26, please delete "OM99-2 and OM99-1" and insert --OM99-1 and  
OM99-2-- in place thereof.

On page 8, line 4, please delete "Figure 2", and insert --Figure 6-- in place thereof.

On page 44, line 15, please delete "Figure 5A", and insert --Figure 4A-- in place thereof.

On page 44, line 18, please delete "Figure 5B", and insert --Figure 4B-- in place thereof.

On page 47, lines 27-28, please delete "A typical protein diffraction pattern is shown in Figure 6."

On page 51, line 5, after "in", please insert --Å--.

On page 51, line 6, after "(" and before the first ",", please insert --α--; before the second ",", please insert --β--; and after "and" and before "in", please insert --γ--.

On page 51, line 7, please insert --Å-- between the parentheses.

On page 51, line 12, after "<I/", please insert --σ--.

On page 51, line 17, please insert --Å-- between the parentheses.

On page 51, line 20, after "(" and before "2", please insert --Å--.

On page 51, line 24, after "=", please insert --Σ--; before "i", please insert --Σ--; and after "/", please insert --Σ--.

On page 51, line 26, after "=", please insert --Σ|--; before "/", please insert --|--; and after "/", please insert --Σ--.

On page 51, line 29, after "F<sub>o</sub>/", please insert --σ--.

On page 52, line 2, please delete "Figure 7", and insert --Figure 6-- in place thereof.

On page 52, line 5, please delete "Figure 7", and insert --Figure 6-- in place thereof.

On page 52, line 7, please delete "Figure 7", and insert --Figure 6-- in place thereof.

On page 52, line 10, please delete "Figure 7", and insert --Figure 6-- in place thereof.

On page 52, line 17, please delete "Figure 7", and insert --Figure 6-- in place thereof.

On page 52, line 20, please delete "Figure 8", and insert --Figure 7-- in place thereof.

On page 52, line 23, please delete "Figure 7", and insert --Figure 6-- in place thereof.

On page 52, line 29, please delete "Figures 7 and 8", and insert --Figures 6 and 7-- in place thereof.

On page 53, line 22, please delete "Figure 9", and insert --Figures 8 and 9-- in place thereof.

On page 54, line 2, please delete "Figure 9", and insert --Figure 8-- in place thereof.

On page 54, line 8, please delete "9", and insert --8-- in place thereof.

On page 54, line 11, please delete "Figure 9", and insert --Figure 8-- in place thereof.

On page 54, line 21, please delete "Figure 9", and insert --Figure 8-- in place thereof.

On page 54, line 29, please delete "Figure 10, and insert --Figure 9-- in place thereof.

On page 55, line 2, please delete "Figure 10", and insert --Figure 9-- in place thereof.

On page 55, line 5, please delete "Figure 10", and insert --Figure 9-- in place thereof.

On page 56, line 2, please delete "Figure 11", and insert --Figure 10-- in place thereof.

On page 56, line 7, please delete "Figure 12", and insert --Figure 11-- in place thereof.

On page 56, line 10, please delete "Figure 13", and insert --Figure 12-- in place thereof.

On page 56, line 13, please delete "Figure 14", and insert --Figure 13-- in place thereof.

On page 56, line 14, please delete "Figure 14", and insert --Figure 13-- in place thereof.

### **In the Claims**

Please cancel claims 1-20.

Please add new claims 24-26.

24. (New) The method of claim 21 wherein the inhibitor is modeled using a computer program based on the crystallization coordinates of memapsin 2.

25. (New) The method of claim 21 wherein the inhibitor is modeled using a computer program based on the parameters for memapsin shown in Table 2.

26. (New) The method of claim 21 comprising creating a data base of data obtained by modeling more than one inhibitor based on the crystallization coordinates of memapsin 2 or parameters of Table 2.

### **Remarks**

This Preliminary Amendment is made to conform the specification to the formal drawings filed herewith. Figure 5 has been relabeled Figures 5A, 5B, 5C, 5D, and 5E to conform to the description of the drawing in the specification. Table 2 on page 51 of the specification has been corrected to add several special symbols that were either unavailable or did not print

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correctly at the time the application was filed. These symbols have been inserted into Table 2.

No new subject matter has been added.

Respectfully submitted,



Patrea L. Pabst  
Reg. No. 31,284

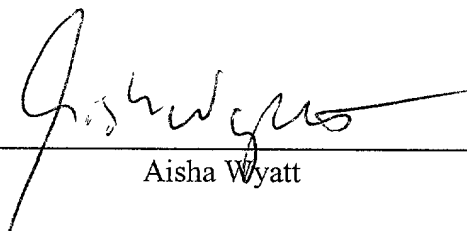
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I hereby certify that this paper and any documents referred to as attached or enclosed are being deposited with the United States Postal Service on this date, April 30, 2001, in an envelope as "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, Mailing Label Number EL 709 418 840 US addressed to Box Patent Application, Assistant Commissioner for Patents, Washington, D.C. 20231.

  
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Aisha Wyatt

Date: April 30, 2001

*Claims As Pending Upon Entry of Preliminary Amendment*

21. A method for treating a patient to decrease the likelihood of developing or the progression of Alzheimer's disease comprising administering to the individual an effective amount of an inhibitor of memapsin 2 having an  $K_i$  of less than or equal to  $10^{-7}M$  or which binds to crystallized enzyme characterized by the parameters in Table 2 when bound to OM-99-2.

22. The method of claim 21 wherein the inhibitor is administered orally.

23. The method of claim 21 wherein the inhibitor blocks cleavage of APP.

24. The method of claim 21 wherein the inhibitor is modeled using a computer program based on the crystallization coordinates of memapsin 2.

25. The method of claim 21 wherein the inhibitor is modeled using a computer program based on the parameters for memapsin shown in Table 2.

26. The method of claim 21 comprising creating a data base of data obtained by modeling more than one inhibitor based on the crystallization coordinates of memapsin 2 or parameters of Table 2.